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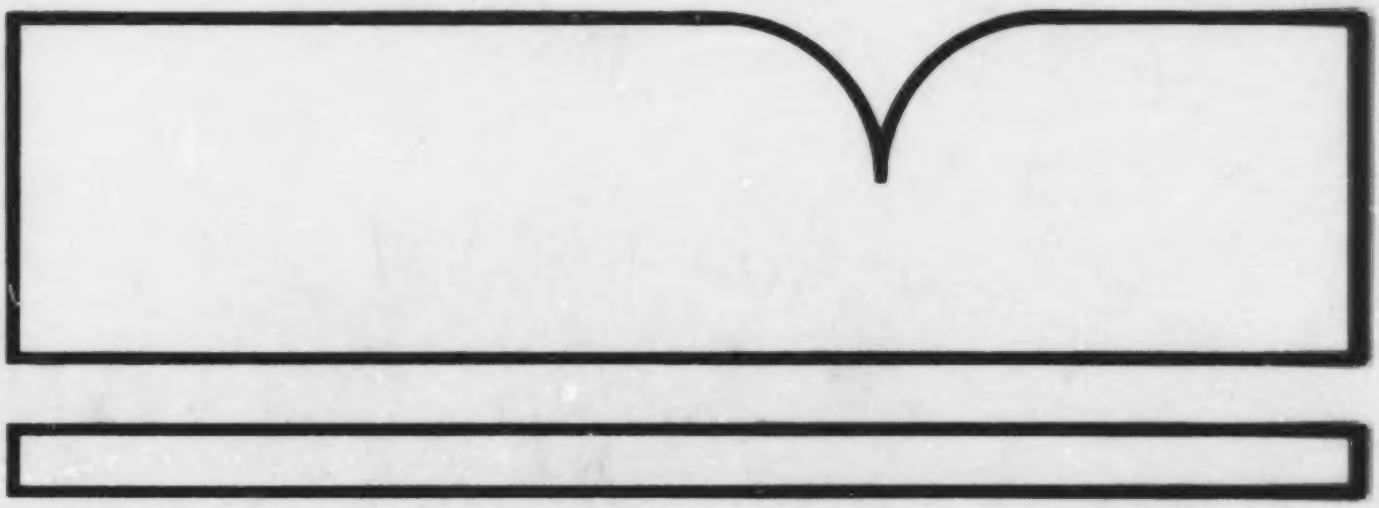

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16. ABSTRACT

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A Comprehensive Cardiac Exercise Stress Processor for Environmental Health Effects Studies*

Mathew L. Petrovick, Paul N. Kizakevich, Ralph W. Stacy, and Edward D. Haak, Jr.

We have shown that an interactive microcomputer system using noninvasive cardiovascular measurements during exercise is both possible and practical. Experimental use of the system has verified our choice of variables as appropriate for automatic generation of a cardiovascular data base, but additional studies are required to determine the system's sensitivity for assessing health-effect decrements.

INTRODUCTION

The effects of air pollutants on the human cardiovascular system have not been well established in environmental medicine.[1-4] A major reason for the lack of a scientific data base has been the absence of suitable biomedical instrumentation to document pollutant dose versus physiological response, especially when conducting exercise cardiovascular studies on the population at risk.[5] Because such information is essential for devising standards for pollution exposure,[6,7] the Environmental Protection Agency (EPA) has undertaken the design of a system that will allow systematic generation of a dose-response data base.

Our clinical objective, then, is to identify the dose-response relationships by analyzing ambient pollutant and physiological covariates. Cardiovascular data should be collected during exercise when airborne pollutant ingestion and tissue oxygen demand increase. Because small, yet cumulative, changes are expected, a comparative trend analysis of exercise response in clean and polluted air is preferred. Since physio-

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logical compensation has been observed in some pollutant studies, a multiparameter trend analysis would be necessary to identify the mechanisms involved.

This paper reports on the design of a cardiac exercise stress processor (CESP) and its features that respond to these clinical objectives. The report is not a conclusive clinical study but an outline of an engineering development expressing the measured parameters, system algorithms, signal-processing techniques, and computations used in quantifying cardiac performance.

BACKGROUND

A system design philosophy was formulated to (1) monitor cardiac electrical and mechanical performance noninvasively during an exercise test; (2) incorporate automated test sequencing, data acquisition, and systems management; (3) employ interactive operation and measurement validation; and (4) implement hardware and software modules that can be modified or expanded.

Cardiac exercise response is usually estimated noninvasively by the electrocardiogram (ECG), which, under stress, may exhibit characteristic changes with cardiac muscle ischemia.[8] Recently, the inaccuracies of assessing the complex cardiac response to exercise by a single measurement criterion (i.e., ST-segment depression $\geq$ 1 mm for 80 msec indicates abnormality) have been identified.[9-11] Accuracy may be improved by including additional ECG measurements[12,13] and independent measures of cardiac performance, such as blood pressure,[14] duration of exercise,[10,15] systolic time intervals,[16-18] and thoracic fluid volume change by electrical impedance measurement.[19]

Cardiac mechanical performance during exercise is measured by several methods; however, most are impractical for our research application. We chose to measure systolic time intervals (STI), which have been studied under a wide range of clinical conditions including exercise stress.[16,18,20-24] The STI include the preejection period (PEP), the left ventricular ejection time (LVET), and the total electromechanical systole (EMS = PEP + LVET). Other associated measurements are the isovolumic contraction time (ICT) and the ratio PEP/LVET.

Methods for obtaining STI measurements include echocardiography;[25] carotid pulse and heart sound,[16] and the first derivative of the thoracic electrical impedance cardiogram (DZ/DT).[26] STI measurement by the impedance method has the advantage of eliminating mechanical transducers. Using only surface electrodes, then, changes in heart rate, rhythm, ischemia, cardiac muscle performance, and thoracic fluid volume can be monitored.

The synchrony of DZ/DT with the intracardiac systolic valvular events was examined by simultaneously recording the ECG, DZ/DT, mitral valve echogram, and aortic valve echogram (Figure 1). Electromechanical systole begins with the ECG Q wave. The anterior (AML) and posterior (PML) mitral valve leaflets close shortly thereafter (T1), which initiates the isovolumic contraction period. At time T2, the aortic valve leaflets (AVL) separate and remain apart until the end of ejection (T3). During ejection, the AVL appear as parallel lines adjacent to the aortic wall (Ao). Following aortic valve closure, the DZ/DT diastolic wave peaks simultaneously (T4) with the maximal mitral valve opening. These independent echocardiographic data illustrate the basis of our STI measurements and support CESP design.

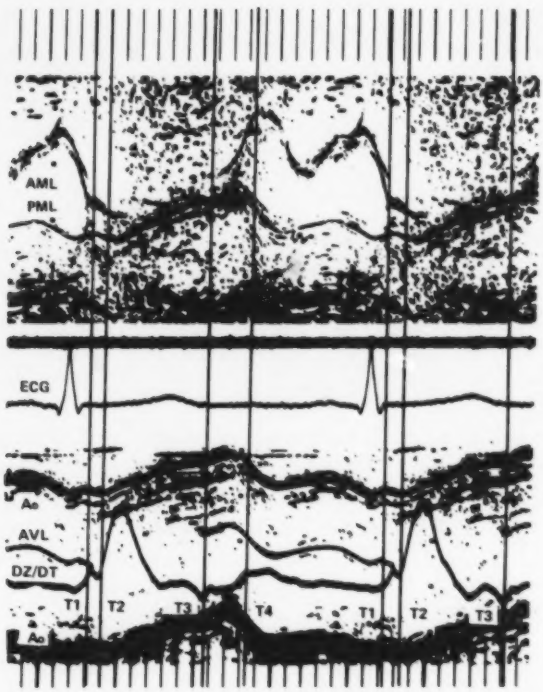

Figure 1. The simultaneous echogram of the mitral valve and the aortic valve illustrates the relation of isovolumic contraction time (T2-T3) and left ventricular ejection time (T2-T3) on the DZ/DT. Abbreviations: anterior mitral leaflet (AML), posterior mitral leaflet (PML), electrocardiogram (ECG), aortic wall (Ao), aortic valve leaflet (AVL).

MATERIALS

The CESP consists of a modified Minnesota Impedance Cardiograph, a custom analogue processor, an Intel System 80/20 microcomputer, and a Lear Seigler ADM-3 interactive graphic display. The Minnesota Impedance Cardiograph (model 304A) was modified to provide a conventional three-lead electrocardiogram. The microcomputer chassis contains an Intel SBC 80/20-4 single-board computer, a Burr-Brown MP 8417 data acquisition system, an Intel double-density diskette subsystem, and an Intel SBC-032 random-access memory (Figure 2).

The analogue processor interfaces between the impedance cardiograph and the microcomputer data-acquisition system. It primarily provides calibration adjustment for each analogue channel and derives the RWAVE signal, which is used for detecting the electrocardiogram QRS event. The ECG is analogue band-pass-filtered (.05–50.0 Hz) to remove respiratory and electrode baseline shifts and to reduce 60-Hz and high-frequency muscle noise. The filtered ECG is passed through a QRS waveform matching filter (7.2–23.4 Hz) to produce the RWAVE event detection signal. The mean thoracic impedance (Z_0) and the impedance cardiogram first derivative (DZ/DT) are bandwidth limited and require only amplitude and baseline adjustment by the analogue processor.

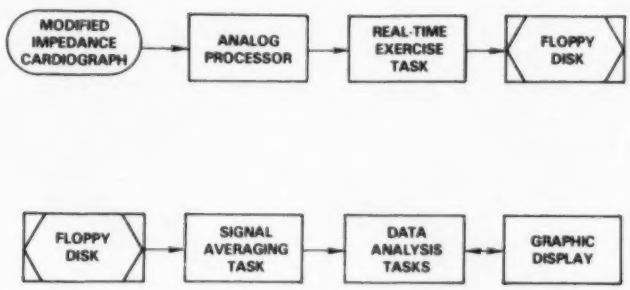

Figure 2. Block diagram of CESP design illustrating segmentation of real-time and postexercise signal processing functions.

For the validation of impedance waveform timing with the echocardiogram, a modified dual-echo IREX model 101 echocardiograph was used. At an operating frequency of 2.25 MHz, an Aerotech 10-mm-diameter transducer for both channels permitted simultaneous mitral valve and aortic valve echograms.

METHOD

The necessity for automated signal processing arises from the complex form in which the clinical information is contained.[20] Certain waveform features must be identified, interfeature amplitude and time measurements made, and clinical indices computed. To achieve these functions, three computer programs were designed: the real-time exercise acquisition program, the systolic time interval analysis program, and the ECG ST-segment analysis program.

The CESP software requirements include interactive graphics, real-time data acquisition, real-time diskette data storage, digital signal processing, waveform analysis, and data base management. Reliability, modularity, structured programming, and self-documentation were also primary considerations, since software changes may be dictated by changing experimental applications. A high-level language (Intel's PL/M-80) was thus chosen for software implementation. The functional information flow among hardware and software systems outlines the CESP processing (Figure 2).

Real-Time Exercise Acquisition

The real-time exercise acquisition program (EXERCISE) manages the real-time data acquisition, coordinates the exercise protocol, and provides the raw data base archival storage. The protocol management processes provide a unique configuration for simultaneous acquisition of STI and ECG ST-segment data during a standardized exercise stress test.

Certain procedures must be followed prior to the stress test. First, the data base diskettes are checked for storage integrity to assure performance during the ensuing stress test. A set of demographic and experimental data is then entered, including pollutant type and dose. These data comprise the initial experimental conditions that are saved in the subject data file.

The second procedure is the graphic verification of the analogue physiological signals. The instrumentation is tested by comparing calibration signals against predetermined calibration levels on the graphic display. The test subject's physiological signals (ECG, RWAVE, DZ/DT, Z_0) are then sampled and displayed against the assumed calibration level (Figure 3) to verify signal amplitude and preexercise (resting) signal quality. The RWAVE is compared to the default trigger level (TRIG) to assure initial triggering, and an error message is displayed if this requirement is not met.

The final procedure is the assignment of exercise protocol. Three data-acquisition protocols are provided by the CESP system: the 12-minute Continuous, the 18-minute Bruce, and the 31-minute ST-segment protocols (Figure 4). For each protocol, the total acquisition period is segmented into stages corresponding to periods of analogue data storage. A total of 12 minutes of real-time data is acquired regardless of the selected protocol, which forms the basis for 12 analysis runs in subsequent data processing. The protocol selection programs the EXERCISE task manager and diskette storage processes for proper sequential operation.

During real-time data acquisition, a heart rate trend display is maintained (Figure 5). The subject's age-predicted maximal heart rate (MAXHR) and 85% of MAXHR are displayed as target end points for patient safety. The display software employs a recursive digital low-pass filter and a transient beat rejection algorithm to present a smooth yet dynamic heart rate trend. The exercise work load within the protocol sequence is controlled by presenting instruction prompts to the operator (Figure 5, lower left). In this manner, the investigator is reminded of the protocol while retaining responsibility and control of patient work load.

Systolic Time Interval Analysis

The systolic time interval analysis program (ANALYSIS) is used for automatic and interactive processing of the raw exercise data. Twelve analysis runs are performed, which correspond to the 12 minutes of data acquisition. The ANALYSIS procedure is basically a cycle of recalling and averaging cardiac cycles, interactive or automatic analysis, and postanalysis variable and averaged-waveform display.

In the automatic mode, these functions are sequenced by the computer, the data are stored, and an exercise response trend of selected clinical indices is displayed. This mode provides a rapid graphic assessment of the experimental results, although some measurement errors may occur. In the interactive mode, the investigator may confirm the waveform feature analysis, adjust waveform features, perform other special operations, and ultimately accept or reject individual runs.

Six waveform feature cursors are displayed: onset of ventricular depolarization [0], closure of the mitral valve [1], opening of the aortic valve [2], time of maximal DZ/DT amplitude [3], closure of the aortic valve [4], and maximal opening of the mitral valve [5].

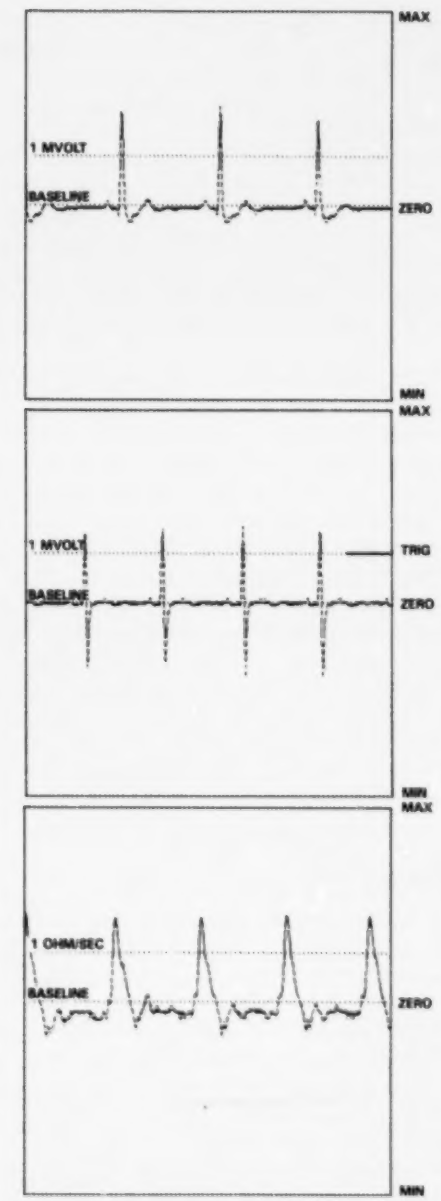

Figure 3. Preexercise validation displays for (A) ECG, (B) RWAVE, and (C) DZ/DT physiological signals.

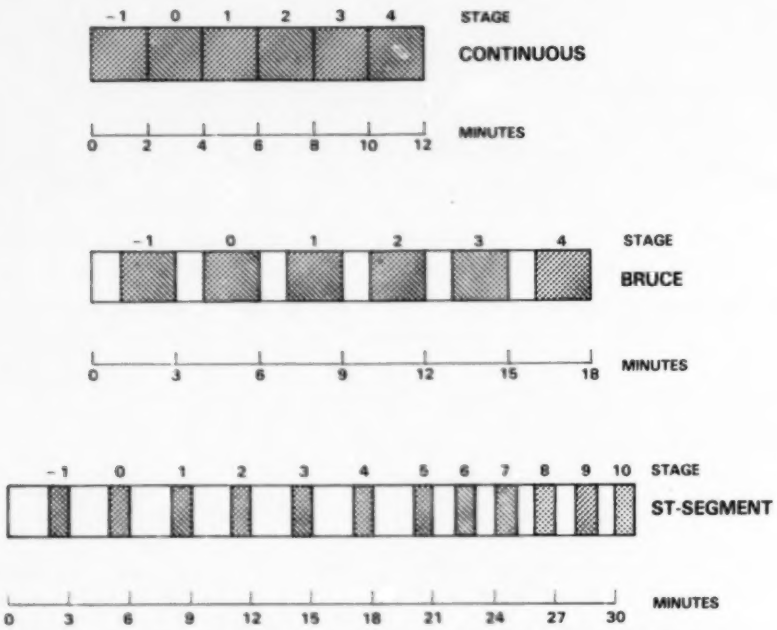

Figure 4. Exercise stress test protocols. Shaded areas indicate real-time data storage.

Consider Figure 6A, in which feature 2 was incorrectly identified by the waveform-processing algorithm. When the cursor number 2 is entered, the cursor is tagged for modification and the next display is generated (Figure 6B). The investigator may now move the cursor to the left or right until the feature is correctly identified, and then lock in the new cursor position. When the investigator validates that all features are correct and no further modifications are required, he may continue to the final interactive display (Figure 6C). At this point, the investigator may accept, flag, or reject the analysis run.

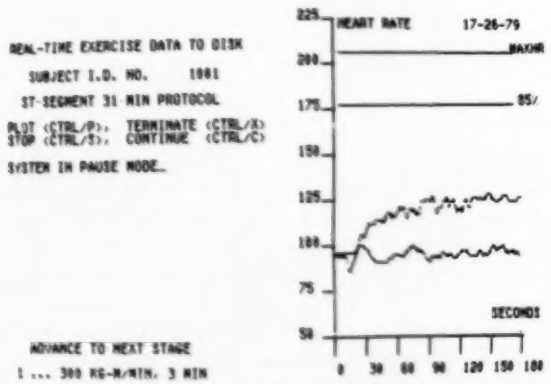

Figure 5. Heart rate trend display during real-time exercise.

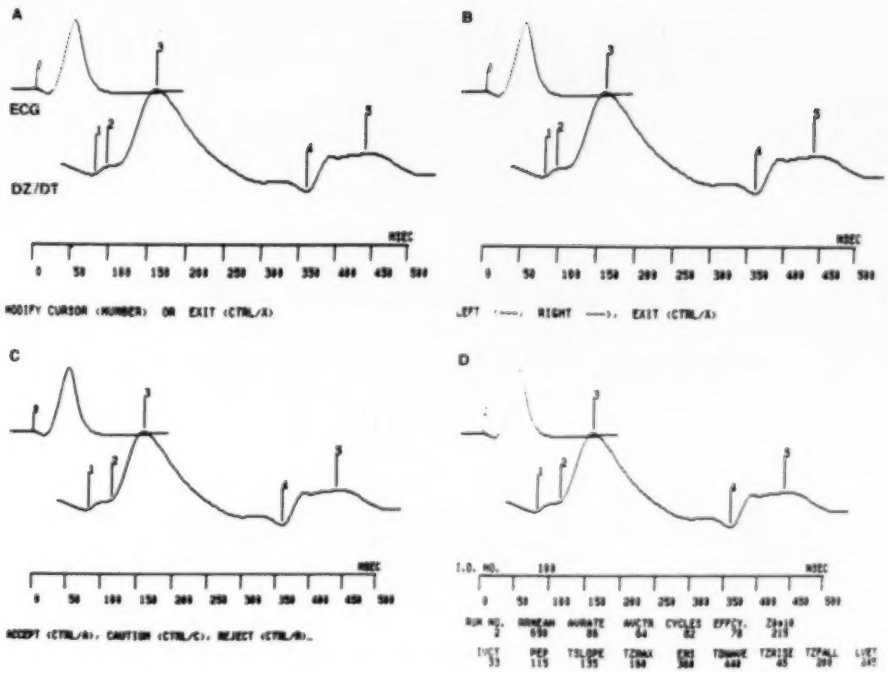

Figure 6. STI analysis interactive graphics displays. (A) ECG and DZ/DT automated cursor placement, (B) interactive cursor movement, (C) clinical data judgment, and (D) derived clinical indices.

When each analysis run is completed, the individual cycle parameters are computed, entered in the postanalysis data array, and displayed (Figure 6D). In the interactive mode, the ensemble-averaged waveforms are then stored on diskette and the current display is maintained until the investigator responds. In the automatic mode, the averaged waveforms are not stored and the current display is maintained only until the next averaging phase is completed (10–20 sec). At the completion of 12 analyses, the postanalysis data array is stored on floppy disk, making a data base of derived clinical indices available for graphic display, statistical analysis, or tabular listing.

ECG ST-Segment Analysis

The ECG ST-segment analysis program (ECGST) processes the 12 ensemble-averaged ECG waveforms for ST-segment analysis. The interactive operational structure is patterned after the ANALYSIS program for consistency. Because the averaged cardiac cycle data file is an output of the ANALYSIS program, the ECGST program requires prior interactive analysis so that investigator-verified waveforms are assured.

For ECG ST-segment analysis, each previously averaged ECG waveform is recalled from disk and a baseline adjustment algorithm is used to compensate for

possible electrode baseline offset. Two simultaneous displays are then presented (Figure 7A). On the left, a time-expanded waveform is drawn with baseline and primary feature cursors, and on the right, the waveform is drawn against a simulated ECG grid. The ECG grid display simplifies the cardiologist's interpretation because of its similiarity to a standard clinical chart recording.

Six waveform feature cursors are displayed: the onset [0] and end [1] of the baseline segment, the onset of ventricular depolarization [2], the peak of the RWAVE [3], and the onset or j-point [4] and end [5] of the ST-segment analysis interval. During manual analysis, baseline onset [0] and/or ST-segment onset [4] may be adjusted. However, the durations of the baseline segment and ST segment are predefined as 20 msec and 80 msec, respectively.

Five clinical indices are derived from the ECG ST-segment analysis (Figure 7B). The DEPRESSION is the mean ECG level calculated over the total ST segment.[8] The SLOPE is the mean ECG slope calculated over the interval between j-point + 10 msec and j-point + 50 msec.[12] The INTEGRAL is the area of the region bounded by the baseline and ECG waveform starting at the j-point and ending at the j-point + 80 msec or at the point when the ECG returns to the baseline, whichever occurs first.[27]

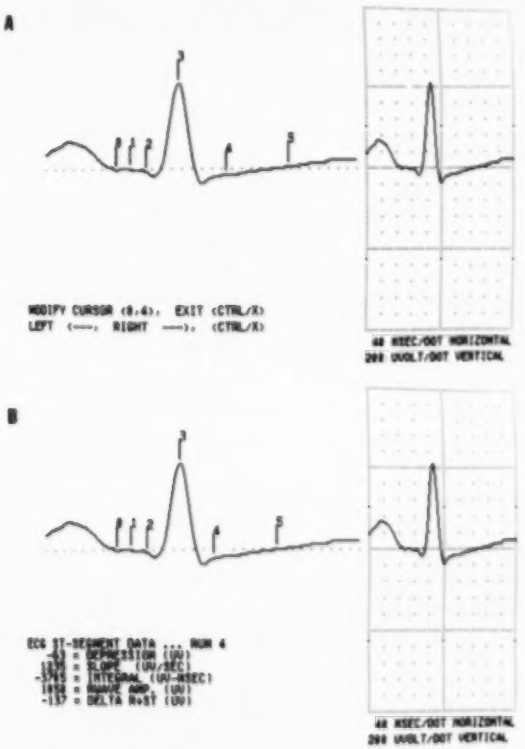

Figure 7. ECG ST-segment analysis interactive graphics displays. (A) automated baseline and cursor placement and (B) derived clinical indices.

The RWAVE AMP is the amplitude of the RWAVE above the baseline.[12] Finally, the DELTA R + ST is the sum of the difference in RWAVE amplitude relative to the control run (number 1) plus the absolute value of the current ST-segment depression.[13]

Each of the 12 ensemble-averaged waveforms is analyzed in sequence and the clinical indices are saved in memory. At the end of ECGST analysis, these indices are merged with the postanalysis data array and saved on floppy disk.

Data Base Design

The purpose of the CESP is to facilitate specific clinical investigations of man's cardiac function when exposed to pollutants. These investigations not only rest upon adequate data acquisition and analysis but also require a comprehensive data base to elicit the varied physiological responses that are anticipated. The CESP data base retains information at each level of the investigation, including experimental conditions, raw analogue samples, averaged waveforms, and measured variables. This structure permits recall, reanalysis, and alternative analysis of the data at any stage, and allows a flexible interpretation of the pollutant dose–response relationship.

Five primary file structures are defined: the subject data file, the real-time RR trend file, the postanalysis data array file, the real-time cardiac cycle data file, and the averaged cardiac cycle data file.

The subject data file contains physiological and other data that describe the experimental conditions of a given exercise test. This file includes subject identification, age, weight, height, sex, and hematocrit. Duration of exercise, protocol mode (Bruce, Continuous, or ST segment), pollutant type, pollutant level, signal sampling frequency, and calibration levels are also included.

During exercise, the average cardiac cycle period is calculated every 30 seconds, and at the completion of exercise, these data are stored in the real-time RR trend file. This file is used to set cardiac cycle acceptance criteria for ensemble averaging and also documents the exercise heart rate response. Following waveform processing, the postanalysis data array file retains the ECG, DZ/DT, and Z_0 measurements, and calculated indices resulting from STI and the ECG ST-segment analysis.

The real-time cardiac cycle data file contains raw data acquired during exercise. Each individual segment contains the sampled ECG and DZ/DT waveforms and other data specific to a single cardiac cycle. The ECG is limited to 160 samples, 64 prior to the RWAVE trigger (160 msec) and 96 after the RWAVE trigger and is limited to 320 samples (800 msec). Specific cyclic measurements include the time since start of exercise, cycle duration (RR interval), exercise stage, and Z_0 sample.

The averaged cardiac cycle data file retains the ECG and DZ/DT ensemble-averaged waveforms for the processed runs. Although the averaged waveforms could be regenerated, storage provides a quick recall for graphic representation of waveform trends. This file uses a first-difference algorithm to conserve storage.

RESULTS

To confirm and document operation, we executed a series of tests using healthy volunteers. Each volunteer performed multistage submaximal exercise on a bicycle

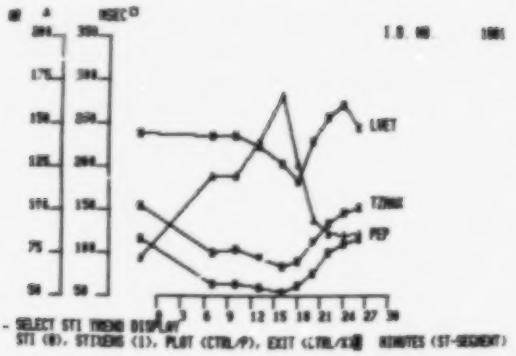

Figure 8. Individual subject's STI exercise response. Heart rate (HRATE), left ventricular ejection time (LVET), time-to-peak DZ/DT (TZMAX), and preejection period (PEP) are illustrated.

ergometer over a load range of 200–700 kg-m/min. The exercise protocols were varied and the system was evaluated in all modes with automatic and interactive analysis. The previous illustrations demonstrate the basic capabilities of acquiring and analyzing the experimental data. Further qualitative assessment can be gained by comparing our data trends with the published literature.

The STI trend display presents the PEP, time-to-peak (TZMAX), LVET, and heart rate (HRATE) as functions of time (Figure 8). Normally, 12 runs are plotted. However, in this experiment, runs 2 and 3 had excessive heart rate variance and were screened out by the artifact rejection software. Nevertheless, a typical exercise stress response was presented.[10,22,23,28,29] PEP and TZMAX shortened significantly and remained constant through the exercise period. LVET decreased linearly with increasing heart rate during exercise, continued to decrease immediately after exercise, and then increased linearly with decreasing heart rate during recovery.[20,28,29]

The subsequent display presents the same time intervals as a percentage of total EMS (Figure 9). This operation cancels the influence of heart rate, especially for

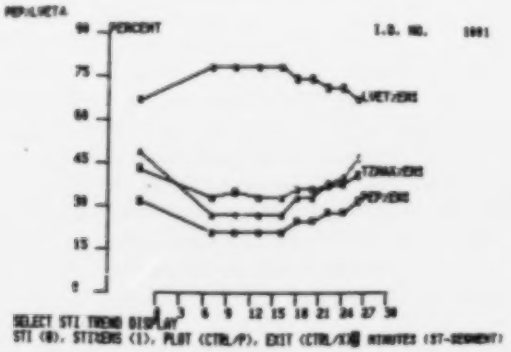

Figure 9. Individual subject's normalized STI exercise response. STI parameters are expressed as a percentage of total electromechanical systole.

LVET.[32] In addition, the conventional ratio of PEP to LVET is expressed as a percentage (PEP%LVET) and plotted. By these transformations, the myocardial inotropic response may be isolated from the heart rate response. Thus, while LVET changed little from control run 1 to exercise run 4, LVET%EMS increased substantially and remained constant throughout exercises.

DISCUSSION

The restrictions of noninvasive assessment of cardiac performance and the need and desire to examine hemodynamic function during exercise leave few alternatives to attain this goal. A further constraint is that the test subjects will be exercising in a controlled environmental chamber and therefore the attending personnel are remote from the subjects and cannot maintain transducer placement. For these reasons, we chose STI measurement by impedance cardiography for cardiac performance assessment. The random motion artifacts associated with impedance cardiography were overcome by ensemble averaging. Hence, the impedance pulse could subsequently serve as a marker for cardiac systolic timing.

A dual purpose is served by giving the investigator responsibility for data integrity. Algorithms for waveform feature identification can never achieve 100% accuracy because waveform quality and configuration may vary. However, the investigator can minimize error by interactive analysis. Second, acceptance and usage of the CESP are expected to be higher because the investigator retains control. At the same time, the mundane management of protocol sequencing and data base contents are controlled by the system.

Since the CESP extends the application of STI measurement beyond most of the reported clinical studies, current interpretation of the exercise response is limited. Clinical studies in the cardiac catheterization and exercise stress laboratories must be performed using both healthy subjects and patients with documented cardiac pathologies. These studies are also required for confirmation of the waveform feature identification accuracy, RWAVE triggering, anomalous beat rejection, artifact screening, and other algorithms subject to intersubject variance. All of this must be done to fully accept and understand the resulting CESP data base.

The CESP serves as a foundation for further expansion as a cost-effective "physiologic data acquisition system" (PDAS) for dedicated environmental health effects studies. Similarly, with appropriate microminiature modifications, the CESP represents a unique design approach for use as an "intelligent personal physiologic monitor"[30,31] as a means of characterizing pollutant health effects in epidemiological studies on the population at risk. The personal monitor approach is a realistic mechanism that can provide the field data base as support for new EPA legislation establishing a preventive environmental medicine program. It is anticipated that CESP dedicated laboratory studies of pollutant health effects will serve as a means of defining epidemiologic criteria for future epidemiological studies of urban populations.

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